Effect of Renal Denervation and Celiac Ganglionectomy on Mean Arterial Pressure in Hypertensive Schlager (BPH/2J) Mice

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ABSTRACT

Renal denervation (RDNx) lowers mean arterial pressure (MAP) in a number of models of hypertension. Less well studied is the effect of celiac ganglionectomy (CGx), a procedure that has proven equally effective at lowering MAP in some animal models. In this study, we hypothesized that RDNx and CGx would both lower MAP in genetically hypertensive Schlager (BPH/2J) mice and that this would correlate with a decrease in sympathetic activity. BPH/2J mice underwent radiotelemeter implantation for monitoring of MAP followed by a 7-10 day convalescence period, after which control data was collected for 2 days. Next, mice were randomly subjected to one of three treatments: RDNx, CGx, or sham. MAP and heart rate were recorded for 14 days post-operatively. Baseline MAP in the three groups was similar (~130mmHg). On post-operative day 14, MAP in both RDNx (-13 ± 2 mmHg) and CGx (-8 ± 0.3 mmHg) decreased, but was not affected in sham controls (-6 +/- 10 mmHg). The change in heart rate (beats/min) was not different between groups 14 days after surgery (-24 ± 4 in sham, -21 ± 33 in RDNx and -41 ± 18 in CGx). To assess the effect of RDNx on renal cytokines in BPH/2J hypertension, tissues were collected from RDNx, CGx, and sham-treated animals two weeks post-treatment in order to confirm the efficacy of the denervations. Future studies will explore the mechanism of how targeted sympathetic ablation changes MAP.

INTRODUCTION

- Renal denervation (RDNx) has been shown to lower MAP in numerous animal models and in hypertensive patients
- Patients with hypertension have high muscle sympathetic nerve activity
- BPH/2J mice have high sympathetic nerve activity
- BPH/2J mice are found to be genetically hypertensive
- The effect of celiac ganglionectomy (CGx) has also been studied in patients and animal models of hypertension, but not as widely

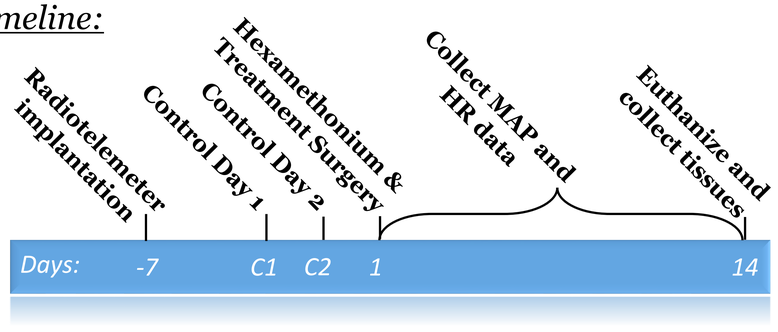
HYPOTHESIS

Renal denervation and celiac ganglionectomy will lower mean arterial pressure (MAP) in BPH/2J mice due to a decrease in sympathetic nerve activity to their respective renal and splanchnic vascular beds.

METHODS

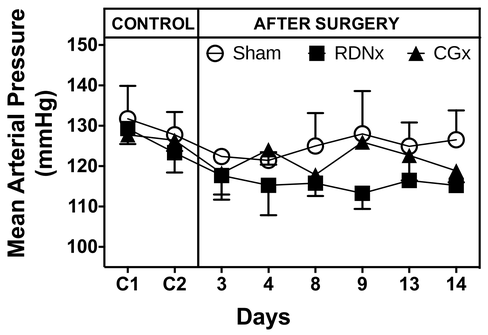
Mice were implanted with radiotelemeters. They were then given a 7-10 day convalescence period, after which baseline MAP and HR data were collected for two days. At the end of control day 2, the mice received injections of hexamethonium (10 mg/kg, IP). After a minimum of 3 hours of recovery, mice were randomly assigned to one of three treatment groups (RDNx, CGx, sham) and underwent the corresponding surgeries. Data was collected for 14 days post-operatively, after which the animals were euthanized. Tissues were collected at this time in order to verify the efficacy of the treatment surgeries using high performance liquid chromatography (HPLC) to analyze the norepinephrine content of the tissues. An effective surgery was one in which the norepinephrine levels had fallen to 10% of control values.

Timeline:

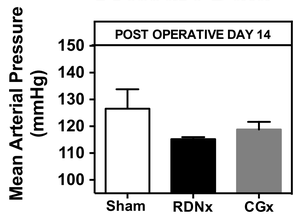


RESULTS

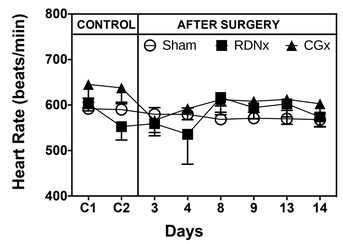
Daily Mean Arterial Pressure Data



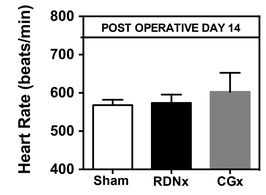
Post-operative Day 14 Mean Arterial Pressure Data



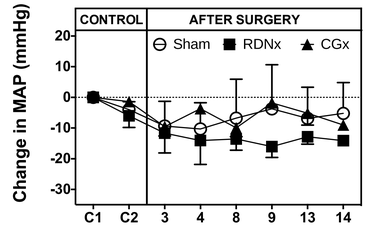
Daily Heart Rate Data



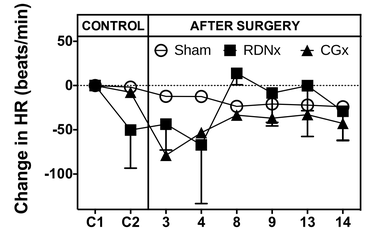
Post-operative Day 14 Heart Rate Data



Daily Change in Mean Arterial Pressure



Daily Change in Heart Rate



SUMMARY

- BPH/2J animals have a high MAP
- RDNx lowers MAP (-13 +/- 2 mmHg)
- CGx also lowers MAP (-8 +/- 0.3 mmHg)
- HR is not affected differently by RDNx, CGx, or SHAM
- After treatments, hexamethonium had a greater drop in pressure for animals in the sham group than RDNx or CGx

CONCLUSIONS

Since RDNx and CGx decreased MAP, we can conclude that the renal nerves contribute to the high baseline MAP in Schlager mice. Sympathetic nerve activity to the kidneys, but not to the splanchnic vascular bed, contributes to MAP regulation in genetically hypertensive Schlager mice.

FUTURE RESEARCH

- Add additional mice to all experimental groups to increase statistical power
- Determine the effect of combined RDNx and CGx
- Explore the role of RDNx and CGx in BPN/3J (normotensive) mice
- Investigate the mechanism of these treatments

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